DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/18/2009 has been entered. Upon entering the submission, claims 1-6 and 18-22 are currently pending.

Information Disclosure Statement

Applicants' Information Disclosure Statement, filed on 05/18/2009, has been considered. Please refer to Applicant's copy of the PTO-1449 submitted herewith.

Response to RCE Submission

Claim rejection under 35 U.S.C. § 102(b)

Applicants' amendment has obviated the rejection.

Claim rejection under 35 U.S.C. § 103a

Applicants amended the rejected claims by further incorporating the limiting steps of resolving racemic (±)duloxetine with di-p-toluyl tartaric acid in a lower alkanol solvent, which achieves an unexpected good result of substantially free of (-)duloxetine at least 94:6 over (+)duloxetine. The previously cited `388 patent does not specifically teach using di-p-toluyl tartaric acid in a lower alkanol solvent for the resolution process. In addition, Applicants' 132 Declaration further demonstrates that (+)duloxetine made in

the cited prior art is only 84% of optical purity, which is much less purer than the purity made by the instant process. In considering all the evidences as a whole, the instantly claimed process is non-obvious over the cited prior art teachings. Therefore, the rejection is withdrawn.

Examiner's amendment

An examiner's amendment to the record with the authorization by Applicants' representative Grant Rodolph dated 07/31/2009 appears below with support in the original specification. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

The application has been amended as follows:

Delete claim 1, and **insert** new claim 1 as follow:

1. (Currently Amended) A process for preparing (+)duloxetine, or an acid addition salt thereof, which process comprises:

(i) resolving racemic (±)duloxetine with di-p-toluyl tartaric acid in a lower alkanol solvent~~a chiral acid~~ so as to obtain a salt of the di-p-toluyl tartaric~~chiral~~ acid and (+)duloxetine, substantially free of (-)duloxetine wherein the ratio of (+) duloxetine: (-) duloxetine is at least about 94:6; and

(ii) if desired, converting the salt prepared in step (i) to the free base or a further acid addition salt.

Delete claims 2 and 3.

Delete claim 5, and **insert** new claim 5 as follow:

5. (Currently Amended) A process for preparing (+)duloxetine hydrochloride, which process comprises:

(i) resolving racemic (±)duloxetine with di-p-toluyl tartaric acid in a lower alkanol solvent so as to obtain (+)duloxetine di-p-toluyl tartrate, substantially free of (-)duloxetine wherein the ratio of (+) duloxetine: (-) duloxetine is at least about 94:6; and

(ii) converting (+)duloxetine di-p-toluyl tartrate prepared in step (i) to (+)duloxetine hydrochloride.

Delete claim 6, and **insert** new claim 6 as follow:

6. (Currently Amended) A process which comprises:

(i) resolving racemic (±)duloxetine with a di-p-toluyl tartaric acid in a lower alkanol solvent ~~chiral acid~~ in a process according to claim 1, and obtaining a mother liquor enriched in (-)duloxetine;

(ii) converting (-)duloxetine obtained from step (i) to (±)duloxetine; and

(iii) if desired, employing (±)duloxetine obtained from step (ii) in a process according to claim 1.

Delete claims 18-22.

Insert new claims 23-28 as follows:

23. (New) The process of claim 1 wherein the lower alkanol solvent comprises ethanol or methanol.

24. (New) The process of claim 1 wherein the lower alkanol solvent is methanol.

25. (New) The process of claim 5 wherein the lower alkanol solvent comprises ethanol or methanol.

26. (New) The process of claim 5 wherein the lower alkanol solvent is methanol.

27. (New) The process of claim 6 wherein the lower alkanol solvent comprises ethanol or methanol.

28. (New) The process of claim 6 wherein the lower alkanol solvent is methanol.

Reasons for Allowance

The present invention is drawn to a process for preparing (+)duloxetine, or an acid addition salt thereof comprising:

1) resolving racemic (±)duloxetine with di-p-toluyl tartaric acid in a lower alkanol solvent to obtain a salt of di-p-toluyl tartaric acid and (+)duloxetine, substantially free of (-)duloxetine wherein the ration of (+)duloxetine:(-) duloxetine is at least about 94:6; and

2) if desired, converting the salt prepared in step (1) to the free base or a further acid addition salt.

The closest prior art of record is *U.S. Patent No. 4,956,388* ("the `388 patent") by Robertson et al.

The `388 patent disclosed a process for preparing (+)duloxetine by resolving the racemic mixture. The `388 patent further taught that this resolution could be carried out in the presence of a resolving agent, such as dibenzoyl -d- and –l-tartaric acids **and the like**. However, the `388 patent did not specifically teach which resolving agent in combination with which specific solvent. In addition, no specific purity was disclosed in the `388 patent, except optical rotation data. According to the instant 132 Declaration, the optical purity based on the data is around 84%, which is much less purer than the purity of at least 94% achieved by the instantly claimed process, comprising steps of resolving racemic (±)duloxetine with di-p-toluyl tartaric acid in a lower alkanol solvent.

Conclusions

- Claims 1, 4-6, and 23-28 are allowed.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Chu, Ph.D, whose telephone number is 571-272-5759. The examiner can normally be reached on 7:00 am - 3:30 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Status Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Yong Chu/
Patent Examiner
Art Unit 1626